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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/832,159	04/10/2001	James Brady		8503

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EXAMINER
DUFFY, PATRICIA ANN

ART UNIT	PAPER NUMBER
1645	6

DATE MAILED: 02/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/832,159	Brady et al
Examiner	**Art Unit**
Patricia A. Duffy	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 16, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-11* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 1-11 are pending and under examination.

2. All of Applicants arguments with regard to the previous rejections of record are moot in view of the new rejections set forth below.

Claim Rejections - 35 U.S.C. § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The teachings of the specification are limited to specific co-polymeric beads that are useful for hemofiltration as taught by the specification. The specification fails to provide written description of a representative number of beads or fibers that include all the relative limitations of the claims and are effective as claimed. No common structural

attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general guidance is needed. Since the disclosure fails to describe the common attributes or structural characteristics that identify members of the genus, and because the genus is highly variant, the relative functions of hydrophobic/hydrophilic; mesoporus/microporus; function of the binding endotoxin or superantigens and cytokines alone is insufficient to describe the genus of particles that function equivalently. One of skill in the art would reasonable conclude that the disclosure of a single copolymer, fails to provide a representative number of species of to describe the claimed genus. Applicants were not in possession of the claimed genus because the specification does not convey to one of skill in the art a representative number of variants in structure and function. The genus of particles with the claimed function is substantial and highly variant because the polypeptides do not have a common structure and function. The recitation of hydrophobic or hydrophilic or other functional terms does not convey a common structure. As such, generic terms that are unrelated via specific structure and function are highly variant and not conveyed by way of written description by the specification at the time of filing. As such, the specification lacks written description for the highly variant genus of functioning particles and one skilled in the art would not recognize that applicants had possession of the genus of particles for use in the hemodialysis system as instantly claimed.

6. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification fails to teach how to make and use the claimed invention. The written description of the specification is limited to two specifically created copyolmers that are treated to have specific physicochemical absorptive characteristics based on the specific chemical composition. The specification fails to teach that these particles are effective to treat infections or sepsis in the manner contemplated by the specification which is withdrawing of blood from the patient, passing it through the system, which includes the hemocompatible blood particulate polymeric material and then returned back to the patient.

The specification does not teach how to make positively charged hydrophobic particles. Example 1 (pages 16-17), of the specification allegedly teaches how to make the "particles of the first group" and "particles of the second group". However, the instructions provided therein can not make the claimed particles and are inconsistent with that set forth in Example 2 (pages 17-18) that also allegedly teach how to make the particles and the particles generated by the first and second methods would necessarily have different pore sizes and different chemical compositions based on the different block polymer structures. It is noted that Example 1, provides for particle sizes and characteristics that do not represent either the first or second claimed particles. In Example 1, in contrast to the claimed invention, the hydrophobic particles is a co-polymer of 2 different monomers (divinylbenzene and ethylvinylbenzene), the selection of which would not result in a positively charged hydrophobic particle as claimed. The chemistry of Example 1, in this specification can not produce a particle that is hydrophobic and positively charged. The ethylenediamine has no corresponding reactive group in the copolymer of divinylbenzene and ethylvinylbenzene to bond to, and as such Example 1, fails to teach how to make a positively charged hydrophobic particle with any the claimed

characteristics. In the method of Example 1, the resultant co-polymer is hydrophobic and not charged and it is not clear form the specification how the surface of the co-polymer is provided with a positive charge. In Example 2, the specification teaches how to make negatively charged particles but that are subsequently coated with polyvinylpyrrolidone (core and shell respectively) and subsequently modified with tetramethyl ethylenediamine to produce a modified particle with a positive charge on the surface of the core. However, this particle is a co-polymer of three distinct individual blocks (divinylbenzene and ethylvinylbenzene and divinylbenzylchloride) which would render the particle hydrophilic and negatively charged and its specific characterization with pore size is not set forth in the specification as filed. The process of co-polymerization is random in nature and the effect of incorporating the divinylbenzylchloride does not necessarily and predictably produce a particle with a hydrophobic core and charged surface. The insertion would be random and the negative charge is present in the interior of the particle and as such, this particle would not have a hydrophobic core as claimed. The teachings of the specification are not clear on how to make this generic particle. The particle of the second group is made as a co-polymer of divinylbenzene and polyvinylpyrrolidone as set forth in Example 1. This co-polymer by virtue of is polyvinylpyrrolidone content would be hydrophilic in nature and not hydrophobic. Co-polymerization produces a random copolymer of the two materials and it is unclear how a core would be produced where the core is hydrophobic. The further the specification teaches that the function of the polyvinylpyrrolidone is to produce a hydrophilic shell in a separate reaction (see page 12, lines 10-13) and it is unclear how this claimed particle is produced given the teachings of the specification. This particle does not have discrete hydrophobic porous core as claimed and the specification as originally filed fails to teach how to make such. Coating is routinely used in the art to describe a "a

layer of one substance covering another". The co-polymerization reaction does not describe a "coating" nor does it describe a neutral hydrophobic mesophorus particle. Further, the specification fails to teach how to make any fibers of either the first group or second group with the recited characteristics. As such, in view of the lack of teaching in the specification of how to make the first and second groups with the claimed characteristics, the unclear teachings with respect to the second group, this specification does not teach how to make and use the claimed particles for use in the blood purification system to treat or prevent sepsis and infection absent further guidance from Applicants.

7. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "hydrophobic, hydrophilic macroporus and mesoporus" in claims 1-11 are relative terms which renders the claims indefinite. The term "hydrophobic, hydrophilic, mesoporus and microporus" are not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Hydrophobic and hydrophilic are not absolutes inasmuch as many compounds have "partial solubility" in water or benzene. There is no definition as what is encompassed by these terms or excluded by these terms. Given the large number of compounds that are "partially soluble" in water, it is unclear as wether these compounds would be considered hydrophobic or hydrophilic. As to "macroporus" and "mesoporus", these terms have substantial overlap in the definitions in the specification and as such there is substantial overlap of macroprous and mesoporus. Therefore one skilled in the art would not be able to determine the metes and bounds of the claim for infringement purposes since there is substantial overlap in the defined sizes

of the pores (see pages 10-11). Are particles pore sizes from 20-50 nm macroporus or mesoporus ?

Claim Rejections - 35 U.S.C. § 102 or 103

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the.effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made

absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 2, 3, 4, 5, 6, 7, 8 and 9 rejected under 35 U.S.C. 102(e) as being clearly anticipated by Matson et al (U.S. Patent No. 6,287,516, filed July 10, 1998).

Matson et al teach a hemofiltration system used to treat inflammatory mediator related disease. Matson et al teach adsorption of the inflammatory mediators from an ultrafiltrate stream that cause inflammatory mediator related diseases to create a post adsorption ultrafiltrate system and combining the utrafiltrate stream with a filtered blood stream and returning the filtered blood/ultrafiltrate to the blood stream mammal (see abstract). The inflammatory mediators of Matson et al include cytokines and endotoxins (column 2, lines 36-65). The hemofiltration system comprises an absorbent device that is comprised of one ore more chambers containing adsorbent material of one or more types in the chamber or chambers. The adsorbent device has a housing and an inlet and outlet means to allow the stream of ultrafiltrate to pass through the device (see Figure 1A, adsorptive device labeled 108). Each chamber may contain an adsorbent or a combination of adsorbent materials. The adsorbent material may be comprised of a host of materials including but not limited to uncharged resins, charged resins, immobilized polymyxin B, anion exchange resin, cation exchange resin, neutral exchange resin, polysuflone, polyacrylonitirle, polymethylmethacrylate, polyvinyl-alcohol, polyamide, polycarbonate, cellulose derivatives etc. The adsorbent material may be organized in a number of ways including a matrix of rods, a porus sieve, a matrix of porous material and beads each

absorbent material may be uncoated or coated (see column 6, lines 32-66). The selection of the adsorbent materials depends upon the inflammatory mediators to be removed. Matson et al therefore teaches any combination of particles, uncharged resins, charged resins and resins that comprise the claimed methylmethylacrylate. As such, the teachings of Matson et al inherently anticipate the claimed invention.

11. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Matson et al, in view of Davankov et al (U.S. Patent No. 5,773,384).

The teachings of Matson et al are set forth supra. Matson et al differs by not teaching a coating of the particle with polyhydroxyethyl methylacrylate, carboxymethylcellulose or polyurethane and do not teach core particles comprised of styrene or vinylbenzne or derivatives thereof.

Davankov et al teach a novel resin for removing blood toxicants comprising a hypercrosslinked styrene resin have a surface modified and heparin electrostatically bound to form an aqueous solution onto the beads with chrlormethyl groups substituted by amino functions through reaction with amines and 2-ethanolamine in particular. Davankov et al also teach other sorbants based on the hydrophobic core and hydrophilic shell structure (see claims 1-13). Additionally, Davankov et al teach a variety of shell structures that provide for chemical modification of the polytyrene resins to enhance hemocompatibility of the material and include copolymers comprising butyl-methylacrylate (see pages 8-9) and polymerization of various hydrophilic monomers, such as hydroxyethylmethacrylate (see page 6) to provide for enhanced biocompatibility. Davankov et al teach sorbents that are styrene-divinylbenzene copolymers (see page 9 of 15).

It would have been *prima facie* obvious to one having ordinary skill in the art to use the sorbents of Davankov et al in addition to the sorbents described by Matson et al in the

adsorbent cartridge of Matson et al because Davankov et al teach that the sorbents are useful for removing blood toxicants. It would have been prima facie obvious to coat any of the adsorbents with a semipermeable polymeric coating such as hydroxyethylmethacrylate or other functional equivalent to provide for enhanced biocompatibility of the sorbents.

Status of Claims

12. No claims are allowed.

13. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 9:30 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.
January 31, 2003

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600